

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Patent application of :
Robert F. Kucharik et al. :
Serial No.: Not Yet Assigned : Group Art Unit:
Not Yet Assigned :
Filed: Herewith : Examiner:
Not Yet Assigned :
For: PHARMACEUTICAL COMPOSITION OF 1- :
(3,4-DIMETHOXYPHENYL)-4-METHYL-5- :
ETHYL-7-METHOXY-8-HYDROXY-5H-2,3- :
BENZODIAZEPINE AND USES THEREOF :

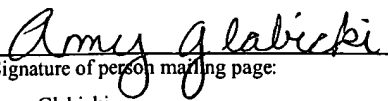
INFORMATION DISCLOSURE STATEMENT

Mail Stop Patent Application
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Pursuant to 37 C.F.R. §1.56 and in accordance with 37 C.F.R. §§1.97-1.98, submitted herewith are copies of the references listed in the accompanying PTO-1449 Forms.

The Examiner is respectfully requested to review the items listed on the attached forms and make them of record in the instant application as required by M.P.E.P. §609. It is requested that the Examiner initial the enclosed duplicate Form 1449, and return one copy to the undersigned.


<p align="center">CERTIFICATE OF MAILING UNDER 37 C.F.R. 1.10</p> <p>EXPRESS MAIL Mailing Label Number: <u>EV 335631195 US</u></p> <p>Date of Deposit: <u>December 3, 2003</u></p> <p>I hereby certify that this correspondence, along with any paper referred to as being attached or enclosed, and/or fee, is being deposited with the United States Postal Service, "EXPRESS MAIL-POST OFFICE TO ADDRESSEE" service under 37 C.F.R. 1.10, on the date indicated above, and addressed to: Mail Stop Patent Application, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.</p> <p align="right"> Signature of person mailing page: <u>Amy Glabicki</u> Type or print name of person</p>
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This Statement should not be construed as a representation that the cited references are material or that more relevant prior art does not exist.

This Statement is being submitted before receipt of any office action on the merits. Thus, no fee is due for the filing of this paper. However, if a fee is due, please charge deposit account 50-0573.

Respectfully submitted,

ROBERT F. KUCHARIK et al.

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SUBSTITUTE FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 18184-0004US	SERIAL NO. Not Yet Assigned
	APPLICANT: Herbert W. Harris et al.	
	FILING DATE Not Yet Assigned	GROUP Not Yet Assigned

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE (IF APPROPRIATE)
	AA	3,736,315	5/29/83	Jéno Kórosi et al.	540	567	
	AB	4,322,346	3/30/82	Jéno Kórosi et al.	540	567	
	AC	4,423,044	12/27/83	Jéno Kórosi et al.	514	221	
	AD	4,614,740	9/30/86	Tibor Láng et al.	514	221	
	AE	4,835,152	5/30/89	Jéno Kórosi et al.	514	220	
	AF	4,840,948	6/20/89	Tibor Láng et al.	514	221	
	AG	5,204,343	4/20/93	Ferenc András et al.	514	221	
	AH	5,288,863	2/22/94	György Somogyi et al.	540	567	
	AI	5,459,137	10/17/95	Ferenc András et al.	514	220	
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	AM	5,891,871	4/6/99	Haiji Xia et al.	514	219	
	AN	6,075,018	6/13/00	Pál Vágó et al.	514	221	
	AO	6,080,736	6/27/00	Donald W. Landry	514	221	

FOREIGN PATENT DOCUMENTS

		DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
	AP	0 492 485 A1	7/1/92	Europe				
	AQ	178516	3/31/83	Hungary			X	
	AR	WO 92/11262	7/9/92	PCT				

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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

AS	F. Gatta et al., "Derivatives of 2,3-Benzodiazepine (*)", Il Farmaco - Ed. Sc. - vol. 40 - fasc. 12, pages 942-955.
AT	R. Sladká et al., "A Placebo-controlled Clinical Trial with Tofizopam * in the Treatment of Anxiety Neurosis" Divisions of Psychiatry, District Institutes of National Health, Prague, 2 and 4; Psychiatric Department and Psychiatric Research Unity, Medical Scholl of Charles University, Prague, Czechoslovakia, pages 176-180
AU	Edit J. Horváth et al., "Anxiolytic 2,3-benzodiazepines, their Specific Binding to the Basal Ganglia", Progress in Neurobiology Vol. 60 (2000), pages 309-342.
AV	E. Tomori et al., "Investigation of the Metabolites of Tofizopam in Man and Animals by Gas-Liquid Chromatography-Mass Spectrometry", Journal of Chromatography, 241 (1982), pages 89-99.
AW	Eva Tomori et al., "Investigation of Metabolites of Tofizopam in Man and Animals", Polish Journal of Pharmacology and Pharmacy, 1984, 36, pages 423-430., PL ISSN 0301-0214.
AX	Sharon Pellow et al., "The Effects of Tofisopam, a 3,4-Benzodiazepine, in Animal Models of Anxiety, Sedation, and Convulsions", Drug Development Research 7, pages 61-73 (1986).
AY	A. Bond et al., "A Comparison of the Psychotropic Profiles of Tofisopam and Diazepam", Eur J Clin Pharmacol (1982) 22, pages 137-142.
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BA	T. Mennini et al., "Brain Levels of Tofizopam in the Rat and Relationship with Benzodiazepine Receptors", Naunyn-Schmiedeberg's Arch Pharmacol (1982) 321, pages 112-115.
BB	K. Maier et al., "The Effect of Tofisopam on Psychic Performance in Persons with More than Average Anxiety: A Controlled Experimental Trial", Current Therapeutic Research, Vol. 35, No. 4, April 1984, pages 541-548.
BC	Chihiro ITO, "Behavioral Pharmacological Study of the Structure-Activity Relationship of Benzodiazepine Derivatives - with Particular Reference to the Activity of 2,3-Benzodiazepine-, (1981) 39(3), pages 369-384 (Japanese), pages 1-30 (English Translation).
BD	Giovambattista De Sarro et al., "GYKI 52466 and Related 2,3-Benzodiazepines as Anticonvulsant Agents in DBA/2 Mice", European Journal of Pharmacology 294 (1995), pages 411-422.
BE	T. Seppälä, "Tofisopam, A Novel 3,4-Benzodiazepine: Multiple-Dose Effects on Psychomotor Skills and Memory. Comparison with Diazepam and Interactions with Ethanol", Psychopharmacology 69, (1980), pages 209-218.

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	BF	Veijo Saano et al., "Tofizopam Modulates the Affinity of Benzodiazepine Receptors in the Rat Brain", Pharmacology Biochemistry & Behavior, Vol. 17, (1982), pages 367-369.
	BG	A. Pakkanen et al., "Comparative Study of the Clinical Effects of Tofizopam, Nitrazepam and Placebo as Oral Premedication", British Journal of Anaesthetics, pages 1009-1012.
	BH	V. Saano et al., "Tofizopam Enhances the Action of Diazepam Against Tremor and Convulsions", Medical Biology 61: (1983), pages 49-53.
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	BK	K. Yamaguchi et al., PMID: 6136319, Abstract of "Tofisopam, A New 2,3-Benzodiazepine. Inhibition of Changes Induced by Stress Loading and Hypothalamic Stimulation", Can. J. Physiol Pharmacol, Vol. 61, (1983), pages 619-625.
	BL	Szegó Judit et al., "Selected Passages From the Clinical-Pharmacological and Clinical Trials of Grandaxin®, "Acta Pharmaceutica Hungarica Vol. 63, (1993), pages 91-98 (Hungarian). Pages 1-10 (English Translation Provided).
	BM	L. Petőcz et al., "The Main Pharmacological Characteristics of Grandaxin (Tofizopam, Egyt-341), Hungarian Medical Journal, Vol. 23, No. 4, (1975), pages 134-138.
	BN	Petőcz Lujza, "The Pharmacological Effects of Tofizopam (Grandaxin)®", Acta Pharmaceutica Hungarica, Vol. 63, (1993), pages 79-82 (Hungarian. Pages 1-4 (English Translation Provided).
	BO	Study of efficacy and safety of Grandaxin tablets for unidentified complaints with digestive system disease. Asano Sadhiro, Orita Yuichi, Kuga Masafumi and Amamor Masanori. Journal of New Remedies & Clinics, 1993, Vol. 42, No. 12, pages 2551-2556. English translation provided.
	BP	Clinical Evaluation of Tofisopam (Grandaxin) on Gastro-intestinal Various Unidentified Complaints. Aoyagi Toshio, Kubo Akiyoshi, Sano Masaaki, Kashiwazaki Kazuo, Kojima Toshiya, Nishizato Yoshinori, Koizumi Kazumasa, Yoshioka Masahiro and Miyake Shozo. Japanese Pharmacology & Therapeutics, 1992, Vol. 20, No. 2, pages 657-667. English translation provided.
	BQ	From actual practice of diagnosis and treatment. Clinical effect of tofisopam (Grandaxin) on unidentified complaints of digestive system. Kitano Atsuo, Okabe Hiroshi, Nakamura Shiro, Obata Akishige, Oshitani Nobuhide, Hioki Masato, Matsumoto Takayuki, Okawa Kiyotaka and Kobaysashi Junzo. Journal of New Remedies & Clinics, 1988, Vol. 37, No. 9, pages 1735-1739. English translation provided
	BR	Effect of Tofisopam (Grandaxin) on irritable colon and cardiac neurosis. Hanajima H. Journal: Yakuri to chiryo. (Japanese pharmacology and therapeutics), 1987, Vol. 15. No. 15, pages 307-217. English translation provided.

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BS	Milena Rizzo, "Chromatographic Separation of 2, 3-Benzodiazepines", Journal of Chromatography B, 747 (2000), pages 203-216.
BT	Miklos Simonyi et al, "Stereoselective Binding of a 2,3-Benzodiazepine to Human Serum Albumin", Biochemical Pharmacology, Vol. 32, No. 12, (1983), pages 1917-1920.
BU	Julia Visy et al., "The Role of Configuration and Conformation in the Binding of 2,3-Benzodiazepines to Human Serum Albumin", CHIRALITY 1 (1989), pages 271-275.
BV	Sergey V. Kalashnikov et al., "Immunomodulating Effects of Tofizopam (Grandaxin®) and Diazepam in Vitro", Mediators of Inflammation, Vol. 11, (2002), pages 53-59.
BW	Fogassy E. et al., "Studies on the Properties and Structure of Optically Active 1-(3,4-Dimethoxyphenyl)-4-Methyl-5-Ethyl-7,8-Dimethoxy-5H-2,3-Benzodiazepine (Tofizopam)", Studies in Organic Chemistry, Vol. 18, (1984), pages 229-233.

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